REMARKS

Claims 31, 32, 43, 44, 63, 64, 90, and 91 are canceled without prejudice or disclaimer because they are essentially duplicative of other claims. Applicants prefer to simplify the claims for prosecution. Claims 51, 56, 78, and 83 are canceled without prejudice or disclaimer because they recite growth hormone secretagogue as an element, yet the respective claims upon which they depend are amended to no longer incorporate growth hormone secretagogue.

Claims 34, 36, 45, 46, 52, 65, 73, 79, and 92 are amended to remove reference to growth hormone secretagogues. As a result, the only claims now pending that cover inventions involving growth hormone secretagogues are newly presented claims 93-108.

New claims 93-108 are submitted under 37 C.F.R. § 1.607 in order to have an interference declared between the subject application and U.S. Patent No. 6,043,026 ("'026 patent"), and any pending continuation or divisional application thereof. A copy of the '026 patent is provided herewith as Exhibit 1, and is cited in the Information Disclosure Statement and Form PTO-1449 filed herewith.

Pursuant to 37 C.F.R. § 1.607(a)(2), Applicants present the following proposed count:

1. Combinations, pharmaceutical compositions, processes of making, and methods of treating or preventing a disease selected from the group consisting of the following:

   (1) combinations according to claims 1-12 of U.S. Patent 6,043,026; or claims 93-96 of U.S. Application No. 736,051;

   (2) pharmaceutical compositions according to claims 13-14 of U.S. Patent

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6,043,026; or claims 103-105 of U.S. Application No. 736,051;

(3) processes for making according to claim 15 of U.S. Patent 6,043,026; or claims 106-108 of U.S. Application No. 736,051;

(4) methods of treating or preventing a disease according to claims 16-21 of U.S. Patent 6,043,026; or claims 97-101 of U.S. Application No. 736,051.

Applicants submit that claims 1-21 of the '026 patent correspond to the proposed count. Claims 93-108 of the instant application correspond to the proposed count and are supported by the specification as follows:

Claim 93

A combination that comprises an estrogen agonist/antagonist and a growth hormone secretagogue.	*Page 1, lines 1-3; page 16, lines 10-11; page 32, lines 26-30.*

Claim 94

The combination of claim 93, wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or its L-tartaric acid salt.	*Page 33, lines 6-8.*

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Claim 95

The combination of claim 93, wherein the estrogen agonist/antagonist is raloxifene or a pharmaceutically acceptable salt thereof. *Page 5, lines 17-18.*

Claim 96

The combination of claim 93, wherein the estrogen agonist/antagonist is (-)-Cis-6-phenyl-5-[4-(2-pyrrolodin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol *Page 21, lines 31-32.*

Claim 97

A method for treating a condition which presents with low bone mass comprising administering to a patient in need thereof a therapeutically effective amount of the combination of claim 93. *Page 4, lines 17-20.*

Claim 98

A method for treating a condition which presents with low bone mass comprising administering to a patient in need thereof a therapeutically effective amount of the composition of claim 94. *Page 4, lines 17-20.*

Claim 99

A method for treating a condition which presents with low bone mass comprising administering to a patient in need thereof a therapeutically effective amount of the combination of claim 95.

Page 4, lines 17-20.

Claim 100

A method for treating a condition which presents with low bone mass comprising administering to a patient in need thereof a therapeutically effective amount of the combination of claim 96.

Page 4, lines 17-20.

Claim 101

The method of claim 97 wherein the condition is osteoporosis.

Page 4, line 19.

Claim 102

A pharmaceutical composition comprising an estrogen agonist/antagonist, a growth hormone secretagogue, and a pharmaceutically acceptable carrier.

Page 4, lines 17-18; page 16, lines 10-12; page 30, lines 2-4; page 47, line 33 to page 48, line 4.

b

Claim 103

The composition of claim 102, wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or its L-tartaric acid salt.

Page 33, lines 6-8.

Claim 104

The composition of claim 102, wherein the estrogen agonist/antagonist is raloxifene or a pharmaceutically acceptable salt thereof.

Page 5, lines 17-18.

Claim 105

The composition of claim 102, wherein the estrogen agonist/antagonist is (-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol or a pharmaceutically acceptable salt thereof.

Page 21, lines 31-32.

b

Claim 106

A process for making a pharmaceutical composition comprising combining an estrogen agonist/antagonist, a growth hormone secretagogue, and a pharmaceutically acceptable carrier.

Page 48, lines 1-3; page 50, lines 21-25; page 51, lines 3-7 and 19-22.

Claim 107

The process of claim 106, wherein the estrogen agonist/antagonist is raloxifene, (-)-Cis-6-phenyl-5-[4-(2-pyrrolidin-1yl-ethoxy)]-5,6,7,8-tetrahydro-naphthalene-2-ol or a pharmaceutically acceptable salt thereof.

Page 48, lines 1-3; page 50, lines 21-25; page 51, lines 3-7 and 19-22.

Claim 108

The process of claim 106, wherein the growth hormone secretagogue is 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or its L-tartaric acid salt.

Page 48, lines 1-3; page 50, lines 21-25; page 51, lines 3-7 and 19-22.

As indicated above, claims 93-108 find clear support in the present application. In addition, each corresponds to the proposed count, as does each claim of the '026 patent. It is respectfully submitted that the remaining claims pending in this application, namely claims 1-4, 6-14, 16-30, 33-

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42, 45-50, 52-55, 57-62, 65-77, 79-82, 84-89, and 92, are patentably distinct from the proposed count.

The effective filing date of the instant application, based on U.S. priority patent application No. 60/012,412, is February 28, 1996, which is prior to the effective filing date of the '026 patent. Accordingly, Applicants request that an interference be declared between the instant application and the '026 patent and any continuing or divisional application thereof and that Applicants be declared the senior party.

Respectfully submitted,

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Appendix
Marked-up Version of Amended Claims
App. Ser. No. 09/736,051

34. (Amended) A pharmaceutical composition comprising:

a. a therapeutically effective amount of a first compound, said first compound being droloxifene, raloxifene, tamoxifen or idoxifene; and

b. a therapeutically effective amount of a second compound, said second compound being sodium fluoride ~~or N-[1(R)-[1,2-Dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide:MK-677~~.

36. (Amended) A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass

a. a therapeutically effective amount of a first compound, said first compound being droloxifene, raloxifene, tamoxifen or idoxifene; and

b. a therapeutically effective amount of a second compound, said second compound being sodium fluoride ~~or N-[1(R)-[1,2-Dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide:MK-677~~.

45. (Amended) A kit containing a treatment for a condition which presents with low bone mass comprising:

a. a therapeutically effective amount of droloxifene, raloxifene, tamoxifen or idoxifene and a pharmaceutically acceptable carrier in a first unit dosage form;

b. a therapeutically effective amount of a sodium fluoride ~~or N-[1(R)-[1,2-Dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide:MK-677~~ and a pharmaceutically acceptable carrier in a second unit dosage form; and

b. container means for containing said first and second dosage forms.

46. (Amended) A pharmaceutical composition comprising:

a. a therapeutically effective amount of a first compound, said first compound being

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

b

(-)-*Cis*-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-1-[6'-pyrrolodinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;

1-(4'-Pyrrolidinoethoxyphenyl)-2-(4"-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol; or

1-(4'-Pyrrolidinolethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline; and

b. a therapeutically effective amount of a second compound, said second compound being sodium fluoride, a parathyroid hormone, or growth hormone ~~or a growth hormone secretagogue~~.

52. (Amended) A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass

a. a therapeutically effective amount of a first compound, said first compound being

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

(-)-*Cis*-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-1-[6'-pyrrolodinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;

1-(4'-Pyrrolidinoethoxyphenyl)-2-(4"-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol; or

1-(4'-Pyrrolidinolethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline; and

b. a therapeutically effective amount of a second compound, said second compound being sodium fluoride, a parathyroid hormone, or growth hormone ~~or a growth hormone secretagogue~~.

65. (Amended) A kit containing a treatment for a condition which presents with low bone mass comprising:

a. a therapeutically effective amount of

Cis-6-(4-fluoro-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

(-)-*Cis*-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol;

Cis-1-[6'-pyrrolodinoethoxy-3'-pyridyl]-2-phenyl-6-hydroxy-1,2,3,4-tetrahydrohaphthalene;

1-(4'-Pyrrolidinoethoxyphenyl)-2-(4"-fluorophenyl)-6-hydroxy-1,2,3,4-tetrahydroisoquinoline;

Cis-6-(4-hydroxyphenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol; or

1-(4'-Pyrrolidinolethoxyphenyl)-2-phenyl-6-hydroxy-1,2,3,4-tetrahydroisoquinoline and a pharmaceutically acceptable carrier in a first unit dosage form;

b. a therapeutically effective amount of sodium fluoride, a parathyroid hormone, or growth hormone ~~or a growth hormone secretagogue~~ and a pharmaceutically acceptable carrier in a second unit dosage form; and

c. container means for containing said first and second dosage forms.

73. (Amended) A pharmaceutical composition comprising:

a. a therapeutically effective amount of a first compound, said first compound being raloxifene, tamoxifen or idoxifene;

and

b. a therapeutically effective amount of a second compound, said second compound being a parathyroid hormone~~,~~ or growth hormone ~~or a growth hormone secretagogue~~.

79. (Amended) A method for treating a mammal having a condition which presents with low bone mass comprising administering to a mammal having a condition which presents with low bone mass

a. a therapeutically effective amount of a first compound, said first compound being raloxifene, tamoxifen or idoxifene;

and

6

b. a therapeutically effective amount of a second compound, said second compound being a parathyroid hormone~~,~~ or growth hormone ~~or a growth hormone secretagogue~~.

92. (Amended) A kit containing a treatment for a condition which presents with low bone mass comprising:

a. a therapeutically effective amount of raloxifene, tamoxifen or idoxifene;

and a pharmaceutically acceptable carrier in a first unit dosage form;

b. a therapeutically effective amount of a parathyroid hormone~~,~~ or growth hormone ~~or a growth hormone secretagogue~~ and a pharmaceutically acceptable carrier in a second unit dosage form; and

c. container means for containing said first and second dosage forms.

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